

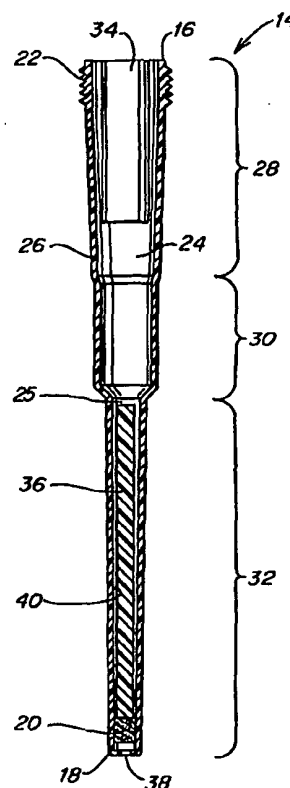
**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup>:</b> <b>B01L 3/02, G01N 35/10</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 98/31465</b> <b>(43) International Publication Date:</b> 23 July 1998 (23.07.98)
<b>(21) International Application Number:</b> PCT/US97/24123 <b>(22) International Filing Date:</b> 31 December 1997 (31.12.97) <b>(30) Priority Data:</b> 08/785,511 17 January 1997 (17.01.97) US <b>(71) Applicant:</b> MATRIX TECHNOLOGIES CORPORATION [US/US]; 44 Stedman Street, Lowell, MA 10851 (US). <b>(72) Inventors:</b> TORTI, Victor, A.; 7 Bear Hill Road, Brookline, NH 03033 (US). KALMAKIS, George, P.; 319 Summer Street, Reading, MA 01867 (US). NELSON, Gary, E.; 97 Irene Drive, Hollis, NH 03049 (US). <b>(74) Agent:</b> MCLANE, Jodi-Ann; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).		<b>(81) Designated States:</b> CA, JP, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i>

**(54) Title:** PIPETTOR INCLUDING AN INDICATOR AND METHOD OF USE**(57) Abstract**

A pipettor including a body portion, a cylinder having an interior channel, and a filter plug disposed within the channel is disclosed. The filter plug may include a plurality of pores and may preferably be treated with a first chemical, so as to affect closure of the pores when the filter plug contacts a pipetted fluid. The pore closure helps contain leakage of the fluid into the pipettor by sealing the pipettor to additional fluid flow. The filter plug may also be treated with a second chemical to affect a change in the color of the filter plug upon contact with the pipetted fluid. The color change acts as a signal to an operator that possible contamination of the pipettor has occurred. The color change and/or closure may also be affected by an aerosol generated from the pipetted fluid.



**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

**PIPETTOR INCLUDING AN INDICATOR AND METHOD OF USE****Background****Technical Field**

5       The present application relates to pipettor and pipetting, and more particularly to a pipettor including an indicator filter.

**Background of Related Art**

Pipettors are widely utilized in laboratories for taking up and discharging precise  
10   quantities of fluid. Automated pipettors generally include a motor for actuating a piston, the piston being housed in a cylinder and open to the tip of the pipettor. Generally, two methods of pipetting are practiced, positive displacement pipetting and air displacement pipetting. In positive displacement pipetting the fluid to be pipetted is in direct contact with the base of the piston and the cylinder in which the piston moves. The piston and walls of the displacement  
15   cylinder of the pipettor are therefore exposed, or contaminated, with the fluid being pipetted, which may be unacceptable in certain applications. Positive displacement pipettors should, therefore, be regularly cleaned or should utilize disposable pistons and cylinders to avoid cross-contamination of samples.

The more common method of pipetting is the air displacement method which utilizes an  
20   air buffer between the base of the piston and the fluid present in a disposable pipette tip, which is attached to one end of the pipettor. In air displacement pipetting, the piston and cylinder in which the piston moves are not intended to be exposed to the fluid being pipetted, as the fluid is generally confined within the disposable pipette tip. Thus, the piston and cylinder need not be replaced or thoroughly cleaned after every use. Even in air displacement pipetting, however,  
25   some contamination of the piston and cylinder may occur if either the fluid itself, or aerosol from the fluid, comes into contact with the piston and/or cylinder. This can occur if the operator inadvertently overfills the disposable tip, or if the fluid is agitated in such a manner as to create aerosol fumes. In such situations the piston and/or cylinder may need to be cleaned or possibly replaced.

30       In some instances it may be difficult for an operator to determine if the cylinder or piston has become contaminated, especially if contamination is due to aerosols formed by the fluid. In

addition, if overfilling has occurred, containing the fluid before it reaches the piston or beyond, would be desirable.

There is therefore a need in the art for a device which indicates contamination of a pipettor to an operator and which helps to limit the extent of overfilling, so as to contain such  
5 contamination.

### Summary

A pipettor including a body portion, a cylinder having an interior channel, and a filter plug disposed within the channel is disclosed. The filter plug may include a plurality of pores  
10 and may preferably be treated with a first chemical, so as to affect closure of the pores when the filter plug contacts a pipetted fluid, thereby sealing the channel containing the filter. The pore closure helps contain further leakage of the fluid into the pipettor by sealing the pipettor to additional fluid flow. The filter plug may also be treated with a second chemical to affect a change in the color of the filter plug upon contact with the pipetted fluid. The color change acts  
15 as a signal to an operator that possible contamination of the pipettor has occurred. The color change and/or closure may also be affected by an aerosol generated from the pipetted fluid.

In one embodiment, the fluid is water or an aqueous based fluid.

In another embodiment, the cylinder includes a tip fitting configured and adapted for use with a disposable pipettor tip.

20 In another embodiment, the cylinder is removably attached to the body portion.

In another embodiment, the filter plug is cylindrical in shape and is friction fitted within the interior channel.

### Brief Description of The Drawings

25 Various embodiments are described herein with reference to the drawings, wherein:

Figure 1 is a schematic of a pipettor including a filter plug in accordance with the present invention;

Figure 2 is an elevation view in partial cross-section of a cylinder including a filter plug of the embodiment of Fig. 1;

30 Figure 3 is an enlarged, perspective view of the filter plug of the embodiment of Fig. 1;  
and

Figure 4 is a schematic of a pipettor containing fluid which has been pipetted and which has passed through the filter plug of the embodiment of Fig. 1 and into the cylinder.

#### **Detailed Description of The Preferred Embodiments**

5 Referring initially to Fig. 1, there is illustrated an automated pipettor 10 utilized for air displacement pipetting and including a body portion 12 and a cylinder 14. Fig. 1 is a representative pipettor only, the embodiment of Fig. 1 being commercially available under the brand name Impact® from Matrix Technologies Corporation, located in Lowell, MA. It should be understood that any number of air displacement pipettor designs, whether manual or  
10 automated, and available from a variety of manufacturers, may be utilized in accordance with the present invention.

With continued reference to Fig. 1 in conjunction with Fig. 2, cylinder 14 includes a first end 16 for connection to body portion 12 and a second, or tip fitting end 18 for connection to a disposable pipette tip 19, the tip fitting end including a filter plug 20 disposed therein. Cylinder  
15 14 may be any of a number of volumes, with volumes of 12.5, 30, 125, 250, and 1250 microliters being conventional, and with a 1250 microliter pipettor being illustrated in the present embodiment. First end 16 preferably includes a threaded section 22 for engagement with corresponding threads (not shown) formed in body portion 12, for releasably securing the cylinder to the body portion. Alternately, other connection methods may be utilized, for example  
20 a bayonet connection, as is well known to one of skill in the art.

Cylinder 14 preferably defines an interior chamber 24 and a communication channel 25, for communication between the pipettor 10 and disposable tip 19. Cylinder 14 may be tapered and include an outer wall 26 having a stepped configuration, as in the illustrated embodiment. The stepped configuration of outer wall 26 may divide chamber 24 into an upper portion 28, a  
25 mid-portion 30, and a lower portion 32, all three portions being in communication with each other. Alternately, cylinder 14 may not have a stepped configuration, or may have greater than, or less than three portions defined by the stepped configuration illustrated in Fig. 2. In the present embodiment, a piston 34 may be actuated to move within chamber 24, between the upper and mid-portions 28, 30 during intaking and dispensing of fluid. The piston 34 preferably does  
30 not enter the communication channel 25 defined by lower portion 32, as the lower portion is preferably elongated, and the channel is therefore preferably smaller than the outer diameter of the piston 34.

Communication channel 25 may include a rod 36 disposed therein, the rod being made of plastic and utilized to take up dead air space, i.e. the air not used in the act of pipetting. Also disposed within channel 25, preferably adjacent tip fitting end 18 and aperture 38, is filter plug 20. In the present embodiment, filter plug 20 is configured and dimensioned to fit within communication channel 25 and may be held in place by friction between the surface of the filter plug and the interior surface 40 of the lower cylinder portion. Alternately, other devices for taking up dead air space, may be utilized, for example, filter plug 20 may be configured and dimensioned to take up the dead air space, as well as performing as an indicator and containment device.

Referring now to Fig. 3, the filter plug 20 may be cylindrically shaped, and preferably is approximately 1/8 to 1/4 of an inch in height, "h", and approximately 1/16 to 1/4 of an inch in diameter, "d". For use in a 1250  $\mu$ l pipettor, filter plug 20 is approximately 1/4 of an inch in height and approximately 1/5 of an inch in diameter. It should be understood that other shapes and sizes are contemplated, provided, however, that the filter plug 20 should be configured and dimensioned to fit within tip section 32. In the present embodiment, the filter plug 20 may be made of a sintered polyethylene material available from General Polymeric of Reading, PA, the material preferably including a plurality of pores, as partially represented by pores 42. Filter plug 20 is preferably treated with a first chemical during compounding and prior to molding, to affect closure of the pores, and may additionally be treated with a second chemical preferably after molding, to affect color change of the plug, both chemicals reacting when the filter plug contacts water or any aqueous fluid. The color change and/or closure may also be affected by an aerosol generated from the aqueous fluid, in the present embodiment. It should be understood that filter plug 20 is preferably chemically treated to react with aqueous fluids because these fluids represent the majority of fluids pipetted. Filter plug 20 may, however, be chemically treated to react to any of a variety of fluids or chemicals, depending upon the desired application. In addition, the filter plug 20 may be treated with either or both of the chemicals, such chemically treated, sintered polyethylene materials also being available from General Polymeric.

Filter plug 20 preferably is composed of a porous, sintered polyethylene material, the sintered polyethylene material being hydrophobic. Prior to contacting water or an aqueous fluid, the plurality of pores 42 allow fluid and air to pass therethrough. Before molding, as part of the compounding process, the polyethylene material is treated with a first, hydrophilic chemical, so that upon contact of the fluid with plug 20, the fluid passes through the pores and initiates a

reaction with the first chemical. This reaction causes the first chemical to close off pores 42 and prevents any further fluid from passing through the plug and into cylinder 14. The filter plug 20 thus acts to contain the fluid and may prevent fluid from contacting the tip of the piston 34, depending upon the amount of fluid which has passed through the filter, and the position of the piston. Filter plug 20 may, additionally, be treated with a second chemical which affects the color of the plug, when the plug contacts the fluid.

Filter plug 20 may preferably be treated with a second chemical, the filter plug being a first color, prior to contact with the fluid. The chemical utilized may selectively change the first color to a second color, upon contact with the fluid, or aerosols generated from the fluid. In the present embodiment, filter plug 20 is preferably treated with a cobalt-chloride which turns the plug a light-blue color, prior to contact with the fluid. Upon contact with water, or any aqueous fluid, the light-blue color changes to a pink color. Alternate chemical treatments and/or colors may be utilized as is known to one skilled in the art. In addition, the first color may be white or clear and the second color may be a shade of the first color. Thus, if during pipetting, fluid inadvertently enters channel 25 through aperture 38, for example by overfilling, the fluid will contact the filter plug 20 and affect a change in color of the filter. This change in color acts as a notification to the operator that the cylinder has contacted the fluid, and that contamination may have, therefore occurred.

In operation, a laboratory technician will choose an appropriate size pipettor 10, the pipettor having a filter plug 20 disposed within communication channel 25. The technician will then choose a disposable tip 19 having a head portion 44 at one end thereof and an aperture 46 at an opposite end thereof, and fit the head portion over the tip fitting end 18, such that aperture 46 is in communication with cylinder 14. The technician is now ready to pipette.

The technician then places disposable pipette tip 19 into a container holding a sample fluid to be pipetted and may input the volume intended to be pipetted, if the pipettor is so designed. The technician then depresses trigger 48 to engage a motor (not shown) disposed within body portion 12, and the motor actuates piston 34. Upon actuation of piston 34, the fluid is drawn into disposable pipette tip 19, and preferably fills the tip to the desired amount. If, however, the fluid overfills tip 19, fluid will enter cylinder 14 through aperture 38, into channel 25 and contact filter plug 20. In the illustrated embodiment, upon contact of an aqueous fluid with filter plug 20, the plug begins to change color from blue to pink and also begins to block its pores 42. As suggested in Fig. 4, once the filter pores are blocked, fluid 50 is trapped above the

filter plug, and no further fluid may flow into the cylinder 14, as the filter plug has been sealed against fluid flow. Thus, filter plug 20 operates as a visual indicator to the operator of possible contamination by changing color and/or operates to prevent further contamination of the cylinder 14 and/or piston 34 by preventing additional fluid from entering the cylinder.

5        It will be understood that various modifications may be made to the embodiment disclosed herein. For example, the filter plug may be treated to only change color and may not block fluid entry, or may only block fluid entry and not change color. In addition, although a single channel pipette is illustrated, the filter plug may be inserted into a channel or tip fitting end of a multi-channel pipettor as well. Therefore, the above description should not be construed  
10 as limiting, but merely as exemplifications of preferred embodiments. Those skilled in the art will envision other modifications within the scope and spirit of the claims appended hereto.



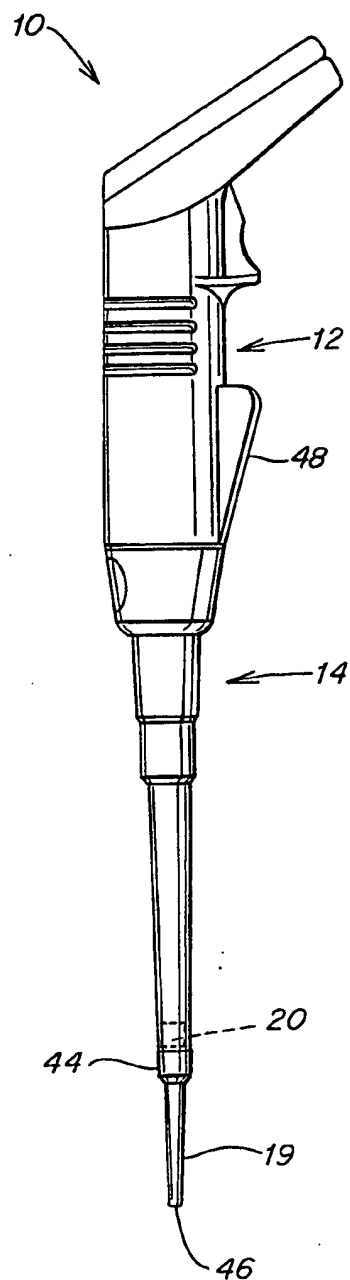
**CLAIMS**

1. An air displacement pipettor for pipetting fluid samples, the pipettor including:  
a body portion;  
a cylinder having a first end attached to the body portion and a second end including an  
5 aperture; and  
a filter plug disposed within the pipettor, the filter plug being changeable from a first  
color to a second color upon fluid entering the pipettor and contacting the filter plug.
2. The pipettor according to claim 1, wherein the filter plug further includes a plurality of  
10 pores in fluid communication with the aperture in the cylinder.
3. The pipettor according to claim 2, wherein the filter plug includes a material which  
blocks the plurality of pores to fluid flow upon a fluid entering the pipettor and contacting the  
filter plug.  
15
4. The pipettor according to claim 3, wherein at least some of the fluid passes through the  
pores and into the pipettor before the pores are blocked.
5. The pipettor according to claim 1, wherein the filter plug is friction fitted within a tip  
20 fitting portion of the pipettor.
6. The pipettor according to claim 5, wherein the tip fitting portion is configured and  
dimensioned for receipt of a disposable tip.
- 25 7. The pipettor according to claim 1, wherein the cylinder is removably attached to the body  
portion.
8. The pipettor according to claim 1, further comprising a piston disposed within the  
cylinder.  
30
9. The pipettor according to claim 1, wherein the pipettor is a multichannel pipettor.

10. The pipettor according to claim 1, wherein the fluid is an aerosol.
11. A pipettor cylinder for attachment to a pipettor, the cylinder including;  
a first end configured and adapted for attachment to a body portion of the pipettor and a  
5 second end including an aperture; and  
a filter plug disposed with the pipettor, the filter plug including a plurality of pores, and  
also including a material which blocks the plurality of pores to fluid flow upon a fluid entering  
the pipettor and contacting the filter plug.
- 10 12. The pipettor cylinder according to claim 11, wherein blocking the plurality of pores seals  
the pipettor to fluid flow.
13. The pipettor cylinder according to claim 11, wherein at least some of the fluid passes  
through the filter plug and into the chamber of the cylinder before the filter plug becomes  
15 hydrophobic.
14. The pipettor according to claim 11, wherein at least some of the fluid passes through the  
pores and into the pipettor before the pores are blocked.
- 20 15. The pipettor cylinder according to claim 11, wherein the filter plug changes from a first  
color to a second color upon fluid contacting the filter plug.
16. The pipettor according to claim 11, wherein the filter plug is friction fitted within a tip  
fitting portion of the pipettor.
- 25 17. The pipettor according to claim 16, wherein the tip fitting portion is configured and  
dimensioned for receipt of a disposable tip.
18. The pipettor according to claim 11, wherein the pipettor is a multichannel pipettor.
- 30 19. The pipettor according to claim 11, wherein the fluid is an aerosol.

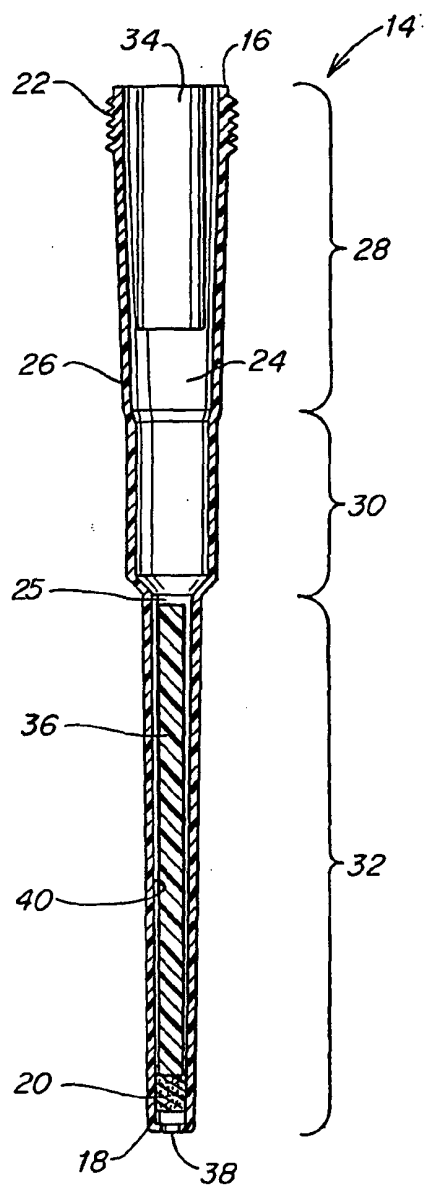
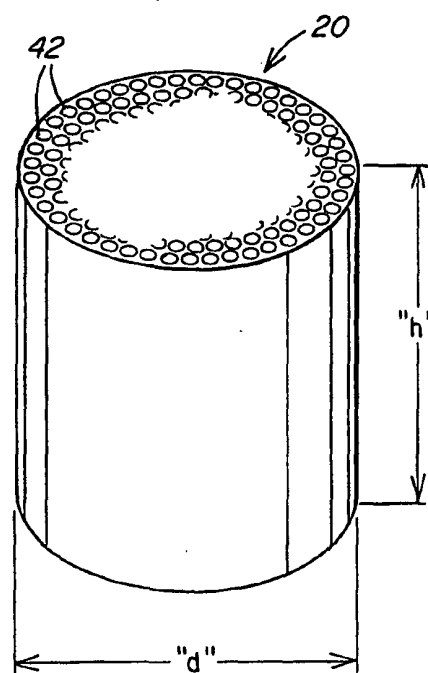
20. A method of pipetting a fluid comprising the steps of:
- providing a pipettor including a body portion, a cylinder including a piston, and a chemically treated filter plug disposed with the pipettor;
  - attaching a pipette tip to the pipettor such that the pipette tip is in fluid communication
  - 5 with the pipettor;
  - actuating the piston such that fluid is drawn into the pipette tip;
  - changing the color of the filter plug from a first color to a second color by contacting the filter plug with the fluid.
- 10 21. The method of pipetting a fluid according to claim 21, further comprising the step of sealing the pipettor from fluid communication with the pipette tip by contacting the filter plug with the fluid.

1/3

**FIG. 1**

RECTIFIED SHEET (RULE 91)  
ISA/EP

2/3

**FIG. 2****FIG. 3**

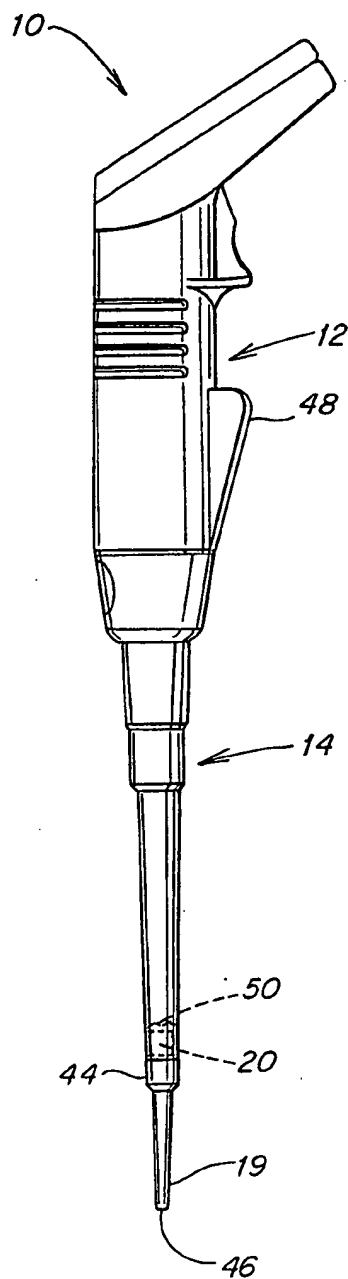


FIG. 4

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/24123

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 B01L3/02 G01N35/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 4 999 164 A (PUCHINGER HERWIG ET AL) 12 March 1991</p> <p>see column 2, line 57 - column 4, line 4 see column 4, line 19 - column 4, line 24 see column 4, line 50 - column 4, line 57 see column 5, line 27 - column 5, line 66 see column 6, line 37 - column 7, line 33 see column 7, line 45 - column 8, line 30 see figures 1-3,5-7</p> <p style="text-align: center;">--- -/-</p>	<p>1-3,5,6, 8,10-12, 15-17, 19,20</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

30 March 1998

Date of mailing of the international search report

06/04/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Koch, A

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/24123

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 5 156 811 A (WHITE DAVID A) 20 October 1992</p> <p>see column 2, line 14 - column 2, line 38</p> <p>see column 2, line 45 - column 2, line 61</p> <p>see column 3, line 18 - column 3, line 47</p> <p>see column 4, line 7 - column 6, line 2</p> <p>see figures 1-6</p> <p>---</p>	11,12, 14,19
X	<p>WO 94 20831 A (WAINWRIGHT NORMAN ET AL) 15 September 1994</p> <p>see page 2, line 28 - page 3, line 36</p> <p>see page 4, line 20 - page 6, line 31</p> <p>see page 9, line 4 - page 9, line 24</p> <p>see page 10, line 5 - page 10, line 20</p> <p>see page 16, line 9 - page 16, line 34</p> <p>see figures 1-3</p> <p>---</p>	1,2,7
X	<p>US 5 364 595 A (SMITH MICHAEL W) 15 November 1994</p> <p>see column 1, line 40 - column 1, line 49</p> <p>see column 1, line 65 - column 2, line 4</p> <p>see column 2, line 20 - column 3, line 56</p> <p>see column 4, line 30 - column 4, line 63</p> <p>see column 5, line 1 - column 5, line 4</p> <p>see column 5, line 31 - column 6, line 11</p> <p>see figure 1</p> <p>-----</p>	11,19



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/24123

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4999164 A	12-03-91	DE 3635598 A DE 3777064 A EP 0264704 A JP 63185457 A	05-05-88 09-04-92 27-04-88 01-08-88
US 5156811 A	20-10-92	NONE	
WO 9420831 A	15-09-94	AU 6360994 A EP 0688426 A	26-09-94 27-12-95
US 5364595 A	15-11-94	CA 2124639 A DE 69407492 D EP 0631817 A JP 7148441 A	03-01-95 05-02-98 04-01-95 13-06-95